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Integration of Flow Chemistry in Multistep Syntheses

Thomas Wirth*[a]

Flow chemistry has become an important tool for synthetic chemists, not only in the academic, heavily research-based environment but also for industrial chemists, who are often faced with the challenge of producing compounds in large quantities. Demands and restrictions such as cost, purity, safety, and accessibility of reagents and starting materials might vary in these two different environments, but flow synthesis allows many of these issues to be addressed. I am very happy that many researchers at the forefront of flow chemistry in academia as well as in industry have contributed to this special issue on multi-step flow synthesis. The **Integration of Flow Chemistry in Multistep Syntheses** is taking standalone flow protocols to the next level by utilizing them either in consecutive flow processes or as part of sequences with batch protocols. Either combination allows taking the highest advantage of flow processes in synthesis and even permits new synthetic strategies to be pursued.



Of the 15 peer-reviewed papers that follow, five Communications and eight Full Papers, as well as two Microreviews contribute to the breadth of the area of flow chemistry. The Microreview by Shinichiro Fuse summarizes recently reported micro-flow photochemical Wolff rearrangements and their application in integrated microflow syntheses. In her Microreview, Tanja Junkers gives a nice overview on the current status of existing characterization methods for monitoring polymerization reactions online. The Front Cover shows the excellent work of David Cantillo and C. Oliver Kappe, the latter contributed two Full Papers to this special issue. The cover picture highlights

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the synthetic sequence towards noroxymorphone, a key intermediate in the preparation of important opioid antagonists. The synthetic route involves an integrated three-step continuous-flow sequence consisting of a hydroxylation followed by hydrogenation and palladium-catalyzed aerobic oxidation. Kappe's second contribution features the synthesis of the racemic amide anaesthetics mepivacaine, rac-ropivacaine, and bupivacaine by using an integrated, continuous-flow tandem hydrogenation/reductive amination strategy. As a Cover Feature, the exciting research of Hiroshi Yasuda and Takahide Fukuyama on the synthesis of [6,6]-phenyl-C61-butyric acid methyl ester (PCBM) is highlighted. The process involves a flow [2+1] addition of C₆₀ and diazoalkane and subsequent flow photoisomerization of the resulting fulleroid to PCBM.

Thank you to all our authors that have undoubtedly worked hard to produce the captivating articles that follow. All these fine contributions are highly inspiring and will form the basis of future developments in this area. Enjoy the flow of this special issue!

Thomas Wirth

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